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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/614,678 | 07/07/2003 | Alexander D. Romaschin | 1148-1-002 CIPF | 7389 |

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| EXAMINER | |
|---|---|
| DUFFY, PATRICIA ANN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 02/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/614,678 | ROMASCHIN ET AL. | |
| | Examiner | Art Unit | |
| | Patricia A. Duffy | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## RESPONSE TO AMENDMENT

The amendment filed 7-9-04 has been entered into the record. Claims 1-20 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Applicants should note that the examiner in charge of the Application has changed. Please address all future correspondence to Exr. Patricia A. Duffy, Art Unit 1645.

All art rejections are withdrawn in favor of the new grounds of rejection set forth below.

### *Rejections Withdrawn*

The double patenting rejections are withdrawn in view of the properly filed terminal disclaimers.

The art rejection over Romaschin et al is withdrawn.

### *Rejections Maintained*

Claims 1-20 stand rejected under 35 USC 103(a) as being unpatentable over DeBaetselier et al (US Patent NO> 4,737,455) in view of Winkelhake et al (Journal of Infectious Diseases, Vol. 165:26-33, 1992) for reasons of record in the last office action.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that DeBaetselier et al dose not teach a measure of oxidants produce by white blood cells present in a reaction in the determination of the quantity of an analyte from a comparison of the oxidant produced by white blood cells because no standard curve relating direct assay readout to analyte level is provided. This is not persuasive. The claims do not specifically require a standard curve as asserted and the standard curve is innate in the quantitative analysis of the agents in biological fluids as specifically contemplated by DeBaetselier et al. Further DeBaetselier et al specifically teach that

light emission is dependent on the dosage providing for both qualitative and quantitative determination of analytes in biological fluids (see column 13, Example 2, 4 and 7). The claims of the '455 patent specifically provide for measuring the presence and proportion of the analyte (see claims 17-24). As such, the patent does teach measuring "an amount". Further "an amount" is any amount and therefore reads on detecting the presence or absence of the analyte in a biological sample. Applicants argue that the claimed invention does not require the addition of the hybrid cells of the patent, yet conversely indicate that the claims encompass such hybrid cells. This is not persuasive, the combination substitutes the cells of Winkelhake et al for the hybrid cells of the '455 patent. Therefore, Applicants are arguing the references individually and not as specifically combined. Applicants argue that the source of the white blood cells may include any combination of those endogenously present in the sample. It is noted that the independent claim is not so limited. Applicants are reminded that the their claim language is open and thus can provide for additional steps and reagents to perform the quantitation. Applicants argue that DeBaetselier et al do not measure oxidants. This is not persuasive; DeBaetselier et al teach that chemiluminescence is probably linked to the formation of unstable oxygen compounds such as superoxides, anions, atomic oxygen and hydrogen peroxide (see column 1, third paragraph; the instant oxidant). Applicants argue that Winkelhake et al does not cure the deficiencies of DeBaetselier et al because DeBaetselier et al does not provide the same inventive concept. This is not persuasive, the arguments with respect to DeBatselier et al were not persuasive and as such the rejection is maintained.

## *New Rejections Based on Amendment*

### *Priority*

It is noted that this instant specification as amended recites particular reference to a PCT application. In particular the passage indicates USSN 08/257,627 is a national

stage filing of PCT/CA94/00325 and which claims priority to Canadian Application Serial No. 2,097,952. A national stage filing of a PCT is filed pursuant to 35 USC 371. USSN 08/257,627 was filed under 35 USC 111. As such, this amended reference introduces new matter into the specification as filed. Further, such an amendment is improper on its face because for benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications and if the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed

to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

It is noted that the record reflects that the reference was not submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required.

The foreign priority claim filed on 7-9-04 was not entered because the foreign priority claim was not filed during the time period set forth in 37 CFR 1.55(a)(1). For original applications filed under 35 U.S.C. 111(a) (other than a design application) on or after November 29, 2000, the time period is during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior foreign application. For applications that have entered national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the claim for priority must be made during the pendency of the application and within the time limit set forth in the PCT and the Regulations under the PCT. See 37 CFR 1.55(a)(1)(ii). If applicant desires priority under 35 U.S.C. 119(a)-(d), (f) or 365(a) based upon a prior foreign application, applicant must file a petition for an unintentionally delayed priority claim (37 CFR 1.55(c)). The petition must be accompanied by (1) the claim (i.e., the claim required by 35 U.S.C. 119(a)-(d) and (f) and 37 CFR 1.55) for priority to the prior foreign application, unless previously submitted; (2) a surcharge under 37 CFR 1.17(t); and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.55(a)(1) and the date the claim was filed was unintentional. The Director may require additional information where there is a

question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the foreign application for patent or inventor's certificate on which priority is claimed pursuant to 37 CFR 1.55, and any foreign application having a filing date before that of the application on which priority is claimed, by specifying the application number, country, day, month and year of its filing.

***Specification***

The amendment filed 7-9-04 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: It is noted that this instant specification as amended recites particular reference to a PCT application. In particular the passage indicates USSN 08/257,627 is a national stage filing of PCT/CA94/00325 and which claims priority to Canadian Application Serial No. 2,097,952. A national stage filing of a PCT is filed pursuant to 35 USC 371. USSN 08/257,627 was filed under 35 USC 111. As such, this amended reference introduces new matter into the specification as filed.

Applicant is required to cancel the new matter in the reply to this Office Action.

***New Rejections***

Claims 8 and 15 are objected to because of the following informalities: MPEP 608.01(m) requires claims to be a full sentence, beginning with a capital letter and ending with a full stop. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995). Where a claim sets for a plurality of elements or steps, each element or step of the claims should be separated by a line indentation, 37 CFR 1.75(i). Applicants are directed to format of claim 1 for acceptable alternatives for multistep claims.

Appropriate correction is required.

Claims 1, 2, 5, 6, 8, 9, 12, 14, 15, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lilius et al (Journal of Bioluminescence and Chemiluminescence, 7:117-122, 1992).

Lilius et al teach a chemiluminescent assay wherein antigen-antibody complexes as well as the capacity of complement to bind these complexes, can be conveniently and rapidly detected in a simple homogenous assay system by using leukocytes as immunosensors without labeling any of the compounds (page 121, column 1, last full paragraph). Lilius et al teach a quantitative non-labeled immunoassay wherein the recognition of antigen-antibody complexes by the Fc-receptors of phagocytic leukocytes and the subsequent activation of the cells. Lilius et al teach activation is proportional to the amount of immune complexes present can be detected by measuring the intensity of chemiluminescence emitted by the activated cells. In addition to the determinations of antigen and an antibody, the binding capacity of complement can be estimated (see page 117, abstract). Lilius et al teach the measurement of the amount of anti-PPase antibodies or the amount of Ppase (i.e. antigen) in a sample using unfractionated leukocytes. The assay involves combining in a single homogenous assay, unfractionated leukocytes, the antibodies in serum containing complement, and the antigen in 500 ul of Hanks balanced

salt solution, luminal, gelatin and varying amounts of antigen and antibody (Figure 1, page 119) . Lilius et al teach standard curves (see page 118, column 2) for quantitation of antigen or antibody. Lilius et al teach that the amount of antigen can be measured in the presence or absence of complement and if complement was present in the assay, an increased assay sensitivity was present. Lilius et al teach that there was no qualitative difference in the assay when either unfractionated or isolated polymorphonuclear or mononuclear leukocytes were used. Lilius et al differ by teaching the presence of the antibody in serum by adding the antigen (i.e. the instant analyte).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to alternatively detect the antigen (i.e. the instant analyte) in a sample of a body fluid such as serum by contacting with the cognate antibody because Lilius et al specifically teach that the amount of antigen can be measured.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lilius et al (Journal of Bioluminescence and Chemiluminescence, 7:117-122, 1992) in view of Winkelhake et al (The Journal of Infectious Diseases, 165:26-33, 1992).

The teachings of Lilius et al are set forth supra. The teachings over Lilius et al as combined supra differ by not assaying for an analyte that is indicative of sepsis in blood.

Winkelhake et al teach glycolipid A is an antigen (i.e. the instant analyte) present in blood in animal models of endotoxemia (i.e. the instant sepsis; page 26, columns 1-2). Winkelhake et al teach monoclonal antibodies that bind pathogenic microorganisms and glycolipid A. Winkelhake et al teach a homogenous chemiluminescent assay wherein the monoclonal antibodies were added to bacteria, incubated to form an opsonic mixture and then combined with a cell/detection mixture comprising unfractionated diluted whole blood containing leukocytes and luminal buffer. Chemiluminescence was detected by adding the opsonic mixture to the cell/detection mixture.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to modify the homogenous chemiluminescent assay of Lilius et al as set forth supra, to assay a body fluid for the sepsis glycolipid A analyte (i.e. antigen) of Winkelhake, using the monoclonal antibodies of Winkelhake et al because Lilius et al teach that the homogenous assay is useful for measuring antigen or antibodies and Winkelhake et al teach that glycolipid A is an important indicator of sepsis. As to claims 3, 4, 10, 11, 16 and 17, it would also have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to modify the assay as modified above to use a whole blood sample comprising both analyte and leukocytes in the chemiluminescent assay as combined directly above, because Winkelhake et al teach that whole blood leukocytes are functional in a luminal-dependent chemiluminescence assay and the use of the leukocytes from a sample of whole blood would reduce the number of steps required to perform the assay, Lilius et al teach that the assay is homogeneous and does not require separation of agents. One would have been motivated to use whole blood as both the origin of the leukocytes and analyte for the assay as combined because it would result in a reduced number of assay steps, simplifying the assay and storage of multiple reagents.

## *Status of Claims*

All claims stand rejected.

## *Conclusion*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy
Primary Examiner
Art Unit 1645